K121033

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SECTION 6
510(k) SUMMARY

This 510(k) Summary is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. The assigned 510(k) number is K121033.

807.92 (a)(1): Name: Ventana Digital Pathology
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SEP 0 6 2013

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Consultant to Ventana Medical Systems, Inc.

807.92 (a)(2): Device name- trade name and common name, and classification

Trade name: Virtuoso™ System for IHC Ki-67 (30-9)

Common Name: Digital pathology and image analysis system for immunochemistry-stained slides

Classifications: 21 CFR § 864.1860- Immunohistochemistry reagents and kits

Product Codes: NOT, NQN, OEO

807.92 (a)(3): Identification of the legally marketed predicate devices

This Virtuoso System for IHC Ki-67 (30-9) is substantially equivalent to its immediate predecessor with the same name, cleared under K111755 on February 22, 2012. The two Virtuoso systems are identical, with the sole difference being the automatic stainer that can be used with the reagents to stain the glass slides. The first Ki-67 submission qualified the Benchmark XT stainer, and this current submission qualified a second automatic stainer, the Benchmark ULTRA stainer.

807.92 (a)(4): Device Description

General Description

The Virtuoso™ System is an instrument-plus-software system designed to assist the qualified pathologist in the consistent assessment of protein expression in immunohistochemically stained histologic sections from formalin-fixed, paraffin-embedded normal and neoplastic tissues. The system consists of a slide scanner (iScan), computer, monitor, keyboard, mouse, image analysis algorithms for

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specific immunohistochemical markers, and software with a Windows web browser-based user interface. Virtuoso is a web-based, end-to-end, digital pathology software solution that allows pathology laboratories to acquire, manage, view, analyze, share, and report digital images of pathology specimens. Using the Virtuoso software, the pathologist can view digital images, add annotations, make measurements, perform image analysis, and generate reports.

Hardware: The iScan slide scanning device captures digital images of formalin-fixed, paraffin-embedded tissues that are suitable for storage and viewing. The device includes a digital slide scanner, racks for loading glass slides, computer, scanner software, keyboard, mouse and monitor.

Software: The Virtuoso software is designed to complement the routine workflow of a qualified pathologist in the review of immunohistochemically stained histologic slides. It allows the user to select fields of view (FOVs) in the digital image for analysis and provides quantitative data on these FOVs to assist with interpretation. The software makes no independent interpretations of the data and requires competent human intervention for all steps in the analysis process.

Additional Materials Required:

- Ventana CONFIRM™ Ki-67 (30-9) rabbit monoclonal primary antibody
- Reagents for visualization, such as universal DAB chromogen
- Associated materials for completing immunohistochemical staining according to the appropriate package insert
- Color printer if user wishes to print color copies

Device Quality Control

The quality of results depends on the laboratory following the quality control instructions recommended in the labeling of the immunohistochemistry (IHC) reagents. The software also performs a quality check on the digital images to determine if they are suitable for further analysis using "Image Quality Assessment" algorithms.

Summary of Procedure

Samples are obtained as formalin-fixed, paraffin-embedded tissue blocks. Histologic sections are prepared and mounted onto glass slides. Slides are reacted with the Ki-67 (30-9) primary antibody, and are then visualized using DAB. Prepared slides are loaded into the Virtuoso system scanner and scanned. The resulting digital images are reviewed by the pathologist on a computer monitor, and appropriate fields of view (FOVs) are then selected for analysis by the Virtuoso software. The Virtuoso software produces a quantitative score for the FOV and an aggregate score over all the FOVs for the whole slide. The

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pathologist has the choice of accepting the result or overriding with his/her own score for some or all FOVs.

807.92 (a)(5): Intended Use

The Virtuoso system provides automated digital slide creation, management, analysis, and viewing. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape.

The IHC Ki-67 (30-9) Digital Read and Image Analysis applications are intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of Ki-67 protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue. Ki-67 results are indicated for use in assessing the proliferative activity of normal and neoplastic breast tissue. When used with Ventana Medical Systems, Inc. CONFIRM™ anti-Ki-67 (30-9) Rabbit Monoclonal Primary Antibody Assay, it is indicated for use as an aid in the assessment of Ki-67 status in breast cancer patients (but is not the sole basis for treatment).

Note: The IHC Ki-67 (30-9) Digital Read and Image Analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and measurement of images from microscope glass slides of breast cancer specimens stained for the presence of Ki-67 protein. The pathologist should verify agreement with the Image Analysis software application score. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRM™ anti- Ki-67 (30-9) Rabbit Monoclonal Primary Antibody assay used to assure the validity of the Virtuoso System for IHC Ki-67 Digital Read and Image Analysis scores. The actual correlation of CONFIRM™ anti-Ki-67 (30-9) Rabbit Monoclonal Primary Antibody to clinical outcome has not been established.

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807.92 (a)(6): Technological Similarities and Differences to the Predicate Devices

The following chart describes similarities and differences between the two test systems.

Characteristic	Virtuoso™ IHC Ki-67 (30-9) [Benchmark ULTRA Stainer]	Virtuoso™ IHC Ki-67 (30-9) [Benchmark XT Stainer] K111755
Intended Use/Indications for Use	This device is intended for in vitro diagnostic (IVD) use. The Virtuoso System provides automated digital slide creation, management, analysis, and viewing. It is intended for IVD use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, size, intensity, pattern and shape. The IHC Ki-67 (30-9) Digital Read and Image Analysis applications are intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of Ki-67 protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue. When used with Ventana Medical Systems, Inc. CONFIRM™ anti-Ki-67 (30-9) Rabbit Monoclonal Primary Antibody, it is indicated for use as an aid in the assessment Ki-67 protein of breast cancer patients (but is not the sole basis for treatment).	SAME SAME SAME
Specimen Type	Formalin-fixed, paraffin-embedded tissue stained by immunohistochemical technique	Same
System Operation (Digital Read and Image Analysis)	Histologic observation by a pathologist through the viewer and image analysis systems	Same
Hardware and Software	Ventana iScan slide scanner, computer, color monitor, proprietary software for Ki-67 (30-9)	Same
Platform Components	mouse, keyboard, windows web browser.	Same
Primary Antibody (Assay) Reagent	Ventana CONFIRM™ Ki-67 (30-9) (reagent is Class I, 510(k) exempt)	Same
Ancillary Reagents/Stainers	DAB universal chromogen kits, Slides stained with Benchmark ULTRA stainer	DAB universal chromogen kits, Slides stained with Benchmark XT stainer
Localization of IHC positive stain	Nucleus	Same
Interpretation	Interpretation is performed by the pathologist.	Same

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807.92 (b)(1/2): Brief Description of Clinical Data (Non-clinical data N/A)

DIGITAL READ PERFORMANCE

The Virtuoso System for IHC Ki-67 (30-9) with the Benchmark ULTRA stainer was clinically validated for digital reading (DR) via a concordance study where 120 cases were evaluated by the manual and DR methods by one pathologist at one site. Each case was scored manually with a routine microscope and as a digital image. The manual score (reference result) was compared to the digital read result.

The data were evaluated as positive or negative for Ki-67 status using 0% to 10% as negative status, and >10% as positive status.

Agreement: Digital Read vs Manual (manual = true score) (ULTRA stainer)
Negative= 0-10%; Positive= >10%

	Manual Microscopic Read		
Digital Read	**Positive**	**Negative**	**Total**
Positive	52	12	64
Negative	0	56	56
Total	52	68	120
Positive Percent Agreement (PPA) n/N (%) (95% CI)	52/52 (100.0) (93.1-100)		
Negative Percent Agreement (NPA) n/N (%) (95% CI)	56/68 (82.4) (71.6-89.6)		
Overall Percent Agreement (OPA) n/N (%) (95% CI)	108/120 (90.0) (83.3-94.2)		

IMAGE ANALYSIS PERFORMANCE

The Virtuoso System for IHC Ki-67 (30-9) with the Benchmark ULTRA stainer was clinically validated for image analysis (IA) via a concordance study where 120 cases were evaluated by the manual and IA methods by three pathologists at three sites. Each case was scored manually with a routine microscope and by using the Virtuoso IA application. The manual score (reference result) was compared to the IA result.

The data were evaluated as positive or negative for Ki-67 status using 0% to 10% as negative status, and >10% as positive status.

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Agreement: Site 1 Image Analysis vs Manual (manual = true score)
Negative= 0-10%; Positive= >10%

	Manual Microscopic Read		
Image Analysis	**Positive**	**Negative**	**Total**
Positive	52	1	53
Negative	25	40	65
Total	77	41	118
Positive Percent Agreement (PPA) n/N (%) (95% CI)	52/77 (67.5) (56.5-76.9)		
Negative Percent Agreement (NPA) n/N (%) (95% CI)	40/41 (97.6) (87.4-99.6)		
Overall Percent Agreement (OPA) n/N (%) (95% CI)	92/118 (**78.0**) (69.7-84.5)		

Agreement: Site 2 Image Analysis vs Manual (manual = true score)
Negative= 0-10%; Positive= >10%

	Manual Microscopic Read		
Image Analysis	**Positive**	**Negative**	**Total**
Positive: >10%	54	2	56
Negative: 0-10%	13	43	56
Total	67	45	112
Positive Percent Agreement (PPA) n/N (%) (95% CI)	54/67 (80.6) (69.6-88.3)		
Negative Percent Agreement (NPA) n/N (%) (95% CI)	43/45 (95.6) (85.2-98.8)		
Overall Percent Agreement (OPA) n/N (%) (95% CI)	97/112 (**86.6**) (79.1-91.7)		

Agreement: Site 3 Image Analysis vs Manual (manual = true score)
Negative= 0-10%; Positive= >10%

	Manual Microscopic Read		
Image Analysis	**Positive**	**Negative**	**Total**
Positive: >10%	59	1	60
Negative: 0 – 10%	10	49	59
Total	69	50	119
Positive Percent Agreement (PPA) n/N (%) (95% CI)	59/69 (85.5) (75.3-91.9)		
Negative Percent Agreement (NPA) n/N (%) (95% CI)	49/50 (98.0) (89.5-99.6)		
Overall Percent Agreement (OPA) n/N (%) (95% CI)	108/119 (**90.8**) (84.2-94.8)		

807.92 (b)(3): Conclusions from Clinical Testing

Concordance studies were performed for the Virtuoso System for IHC Ki-67 (30-9) with the Benchmark ULTRA stainer. The overall agreement between the digital read and the manual read at one site was 90.0%, and the overall agreements between image analysis and the manual read across three sites were 78.0%, 86.6%, and 90.8%, and the predetermined acceptance criterion for each measurement of 75% has been met.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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VENTANA MEDICAL SYSTEMS INC.
C/O MS. ERIKA AMMIRATI
CONSULTANT
575 SHIRLYNN COURT
LOS ALTOS CA 94022

September 6, 2013

Re: K121033
Trade/Device Name: Ventana Virtuoso System for IHC Ki67 (30-9)
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistochemistry reagents and kits
Regulatory Class: II
Product Code: NQN, NOT, OEO
Dated: August 21, 2013
Received: August 22, 2013

Dear Ms. Ammirati:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Maria M. Chan -S

Maria Chan, PhD
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K121033.

Device Name: Virtuoso™ System for IHC Ki-67 (30-9)

Indications For Use:

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Prescription Use ___X___ (Part 21 CFR 801 Subpart D)	AND/OR	Over-The-Counter Use _____ (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH; Office of In Vitro Diagnostics and Radiological Health (OIR)

Maria M. Chan -S

Division Sign-Off
Office of In Vitro Diagnostics and Radiological Health

510(k): k121033